REMARKS

Claims 1-5 are hereby restricted so as to specify pyrophosphate as the ligation by-product, by incorporating the terms of previous claim 13. Claim 7 and claim 13 are cancelled herein. The informalities noted by the Examiner have been remedied, and the rejections under 35 USC § 112 have been addressed, resulting in minor amendments of all claims (cf. listing of claims).

The Applicant submits that Grossman is irrelevant for the present invention, as it relates purely to an improved oligonucleotide ligation assay (OLA), reliant on a completely different detection method. Grossman does provide a nucleic acid sample comprising genetic material, complementary oligonucleotides, and annealing and subsequent ligation of said oligonucleotides. However, in response to paragraph 7 A (e) of the Office Action dated 29 July 2009, Grossman does not teach the detection of a by-product, and specifically not pyrophosphate, from the ligation reaction, but in fact teaches the detection of the actual product, i. e. the oligonucleotide probes ligated together. The present invention teaches the detection of a by-product released as a result of the incorporation of nucleotides during the ligation reaction, and not the ligated product itself (as can be seen from paragraph 33 of the specification). Thus, as novel claim 1 and all subsequent claims cannot be considered anticipated by Grossman, the applicant respectfully requests that the rejections based on Grossman shall be cancelled.

With regard to the anticipation rejections based on the repetitive expansion detection method disclosed in Schalling, the Applicant again asserts that Schalling relies on an entirely different detection principle, where hybridized oligonucleotides are ligated together and where the resulting multimers, i. e. the ligation products, are detected by electrophoresis. Thus, in response to the examiner's standpoint presented in paragraph 7 B (e), the applicant again maintains that the detected product in Schalling is not a ligation by-product but the actual product of the ligation. Thus, in the light of both the above reasoning and the specification of pyrophosphate as the by-product, the applicant respectfully requests that the rejections based on Schalling shall be cancelled.

As pyrophosphate is introduced in claim 1 as the ligation by-product to be detected, the Applicant maintains that the anticipation rejections based on Jansson should be cancelled. In response to the Examiner's rejection of claim 13 based on Jansson (paragraph 7 C (e), second last paragraph on p. 7 of the office action), the Applicant respectfully wishes to clarify that the disclosure of pyrophosphate on p. 2, paragraph 0019 of Jansson, and elsewhere, merely relates to pyrophosphate as one of the products of various enzymatically catalyzed reactions, and not as a by-product for

detection. Therefore, the Applicant respectfully requests that the rejections based on Jansson be cancelled.

With regard to the anticipation rejections based on Schultz, the Applicant asserts that Schultz is not concerned with detection based on ligation by-products, as the analytes are identifier nucleotides, released through depolymerizing activity, and not ligation by-products. Further, as claim 1 of the present invention is amended so as to recite pyrophosphate instead of a ligation by-product, the Applicant respectfully requests that the rejections based on Schultz be cancelled. The Examiner's rejection of claim 13 based on Shultz (paragraph 7 D (e), second paragraph p. 9) is again, in our opinion, a result of a misinterpretation of the cited teaching; since pyrophosphate is only disclosed as a product resulting from the luciferase-mediated catalysis of luciferin and not as a by-product for detection.

The present invention as currently claimed is also not obvious to the person of ordinary skill in the art. Starting from close prior art Jansson *et al.*, it teaches a method for detecting ligase-catalyzed joining of nucleic acid ends, where the detection is based on the release of AMP. The difference between Jansson *et al.* and the present invention as currently claimed is that the present invention employs pyrophosphate as the ligation by-product to be detected. Utilizing pyrophosphate instead of AMP in the detection implies that the method is more versatile, as different enzymatic reactions relying on different substrates for conversion into ATP (for instance pyruvate phosphate dikinase as the enzyme, with the reactants being AMP, PPi, and phosphoenolpyruvate, or ATP-sulfurylase as the enzyme, with PPi and APS as the reactants) can be utilized. This method for determining the presence of a specific genetic element is surprisingly more versatile.

In the event there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

No additional fees are believed to be due at this time however if necessary to effect a timely response the Commissioner is authorised to deduct the necessary fees from Deposit account No. 501249.

Respectfully submitted,

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